

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

- 1 1. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein
2 comprising
3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;
5 and
6 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
7 binds to a protein overexpressed on the surface of a cell.
- 1 2. (Original) The nucleic acid of claim 1, wherein the matrix
2 metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9
3 (gelatinase B) and membrane-type1 MMP (MT1-MMP).
- 1 3. (Original) The nucleic acid of claim 1, wherein the plasminogen activator
2 is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase
3 plasminogen activator (u-PA).
- 1 4. (Previously Presented) The nucleic acid of claim 1, wherein the matrix
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID
3 NO: 20).
- 1 5. (Previously Presented) The nucleic acid of claim 1, wherein the
2 plasminogen activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID
3 NO: 23), GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1 6. (Original) The nucleic acid of claim 1, wherein the protein overexpressed
2 on the surface of a cell is a receptor.

1 7. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide comprises a cytokine.

1 8. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide comprises a growth factor.

1 9. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide is a member selected from the group consisting of: IL-2, GM-CSF, and EGF.

1 10. (Original) The nucleic acid of claim 1, comprising the nucleotide
2 sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1 11. (Original) A vector comprising the nucleic acid of claim 1.

1 12. (Original) The nucleic acid of claim 6, wherein the cell is a cancer cell.

1 13. (Original) The nucleic acid of claim 7, wherein the heterologous
2 polypeptide comprises GM-CSF.

1 14. (Original) The nucleic acid of claim 7, wherein the heterologous
2 polypeptide comprises IL-2.

1 15. (Original) The nucleic acid of claim 8, wherein the heterologous
2 polypeptide comprises EGF.

1 16. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein
2 comprising

3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and

(2) GM-CSF.

17. (Original) A polypeptide encoded by the nucleic acid of claim 1.

18. (Original) A polypeptide encoded by the nucleic acid of claim 10.

19. (Original) A polypeptide encoded by the nucleic acid of claim 16.

20. (Original) A host cell comprising the vector of claim 11.

21. (Original) The nucleic acid of claim 12, wherein the cancer is leukemia.

22. (Original) The nucleic acid of claim 12, wherein the cancer is acute
myelogenous leukemia.

23. (Original) A pharmaceutical composition comprising the protein of claim
18 and a pharmaceutically acceptable carrier.

24. (Currently Amended) A method of treating cancer, the method
comprising administering to a subject a Diphtheria toxin fusion protein comprising
(1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;
and

(2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
binds to a protein overexpressed on the surface of a cancer cell.

25. (Original) The method of claim 24, wherein the matrix metalloproteinase
is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and
membrane-type1 MMP (MT1-MMP).

26. (Original) The method of claim 24, wherein the plasminogen activator is
selected from the group consisting of t-PA and u-PA.

27. (Previously Presented) The method of claim 24, wherein the matrix metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID NO: 20).

28. (Previously Presented) The method of claim 24, wherein the plasminogen activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23), GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

29. (Original) The method of claim 24, wherein the protein overexpressed on the surface of a cell is a receptor.

30. (Original) The method of claim 24, wherein the cell is a cancer cell.

31. (Original) The method of claim 24, wherein the heterologous polypeptide comprises a cytokine.

32. (Original) The method of claim 24, wherein the heterologous polypeptide comprises a growth factor.

33. (Original) The method of claim 24, wherein the fusion protein is encoded by the nucleotide sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

34. (Original) The method of claim 30, wherein the cancer is leukemia.

35. (Original) The method of claim 30, wherein the cancer is acute myelogenous leukemia.

36. (Original) The method of claim 31, wherein the heterologous polypeptide comprises GM-CSF.

37. (Original) The method of claim 31, wherein the heterologous polypeptide comprises IL-2.

1 38. (Original) The method of claim 32, wherein the heterologous polypeptide
2 comprises EGF.

1 39. (Original) The method of claim 24, wherein the Diphtheria toxin fusion
2 protein comprises:

- 3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and
5 (2) GM-CSF.

1 40. (Currently Amended) A method of targeting a compound to a cancer cell
2 overexpressing a cytokine receptor or a growth factor receptor, the method comprising the steps
3 of:

4 administering to the cell Diphtheria toxin fusion protein comprising

- 5 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
6 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and
7 wherein the Diphtheria toxin is cleaved by a matrix metalloproteinase or a plasminogen
8 activator; and

9 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
10 binds to a cytokine receptor or a growth factor receptor.

1 41. (Currently Amended) The method of claim 40, wherein the cell ~~also~~
2 overexpresses a matrix metalloproteinase, a tissue plasminogen activator, or a urokinase
3 plasminogen activator.

1 42. (Original) The method of claim 40, wherein the matrix metalloproteinase
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and
3 membrane-type1 MMP (MT1-MMP).

1 43. (Original) The method of claim 40, wherein the plasminogen activator is
2 selected from the group consisting of t-PA and u-PA.

1 44. (Previously Presented) The method of claim 40, wherein the matrix
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ SEQ ID
3 NO: 20).

1 45. (Previously Presented) The method of claim 40, wherein the plasminogen
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1 46. (Original) The method of claim 40, wherein the cancer cell is a leukemia
2 cell.

1 47. (Original) The method of claim 40, wherein the cancer cell is an acute
2 myelogenous leukemia cell.

1 48. (Original) The method of claim 40, wherein the Diphtheria toxin fusion
2 protein comprises
3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and
5 (2) GM-CSF.

1 49. (Currently Amended) An isolated nucleic acid comprising the sequence
2 set forth in any one of ~~SEQ ID NOS: 2-18~~ SEQ ID NOS: 2-13 or SEQ ID NOS: 15-18.